

**REMARKS/ARGUMENTS**

Claims 1-16 are pending in the instant application. Applicants have amended claim 1. The following remarks are believed to be fully responsive to the Office Action.

**Claim Rejections – 35 USC § 102**

Claims 1, 2, 6, 10, 11, 13 and 14 stand rejected under 35 USC §102(b) as being anticipated by Budsky et al. (CS272584B1).

Budsky teaches a method of the preparation of cyclic anhydrides of DTPA where pyridine is added in a molar amount of 2.48 and acetic anhydride is added in a molar amount of 2.46 per mol of DTPA. Budsky, however, notes that there are shortcomings of the method where DTPA was prepared by the action of acetic anhydride and pyridine. His invention and elimination of the shortcomings is to react acetic anhydride with the aminopolycarboxylic acid deprived of all metal cations in a medium of dioxane and pyridine under the catalytic action of N-dimethyl-4-aminopyridine at 70°C and notes that the reaction time is shortened to 8 hours with a yield of 100%, see page 2, lines 11 to 17 of Budsky. Budsky employs an additional solvent dioxane and also an additional base, N-dimethyl-4-aminopyridine, in his invention.

Applicants have amended claim 1 to specify that pyridine is the sole organic base employed in the present invention.

In view of the Examiner's points 3 -4 made on page 2 of the Office Action dated October 1, 2008 ("Office Action"), Applicants now believe that claims 1, 2, 6, 10, 11, 13, and 14 are in condition for allowance and respectfully request that the Examiner's rejections for claims 1, 2, 6, 10, 11, 13, 14 under 35 USC §102 (b) be withdrawn.

**Claim Rejections – 35 USC § 103(a)**

Claims 1, 2, 6 – 11 and 13 - 15 stand rejected under 35 USC 103(a) as being unpatentable over Budsky et al. (CS272584) in view of Dazzi (US 3,660,388) or Gibby (US 4,822,594).

Budsky teaches that to eliminate the shortcomings with the known process, acetic anhydride is reacted with the aminopolycarboxylic acid in a medium of dioxane and pyridine under the catalytic action of N-dimethyl-4-aminopyridine at 70°C. Budsky uses pyridine in an amount of 2.48 mol per mol of DTPA. Budsky however employs the additional solvent dioxane and also the additional base N-dimethyl-4-aminopyridine in the reaction. The base N-dimethyl-4-aminopyridine also acts as a catalyst as does pyridine. Although Budsky teaches that it is possible to reduce the amount of pyridine in the reaction, he does this by employing additional reagents. The objective of the inventors of the present application was to provide a process for the production of DTPA-bis(anhydride) which involves a minimum of reactants, see page 2, lines 14 to 15 of present application (published international application WO 2005/058846). Budsky therefore proposes an entirely different solution to the problem of optimizing the preparation of DTPA bis-anhydride than the inventors of the present invention and teaches away from the invention of the present application.

Applicants were aware of the technology described by Dazzi prior to the present invention and directs Examiner's attention to page 1, lines 20 to 27 of the description in the present application (published international application WO 2005/058846). Applicants therefore fully agree with the Examiner that at the time of the invention it was obvious to one ordinarily skilled in the art to utilize acetic anhydride and pyridine in the process for the production of DTPA-bis(anhydride) without the use of acetonitrile. However, Dazzi does not disclose less than 6.5 moles of pyridine per mole of DTPA and does nowhere teach or indicate that it would be possible to reduce the amount of pyridine to an amount below this value.

The combined teachings of Dazzi and Budsky teaches to one ordinary skilled in the art that in order to reduce the amount of pyridine in the reaction below the amount taught by Dazzi, one would have to employ additional solvents such as dioxane and an additional

reaction acceleration such as N-dimethyl-4-aminopyridine. Dioxane is a solvent which is known to be toxic. Hence, according to page 2, lines 14 to 16 of the description of the present application (published international application WO 2005/058846), it was an objective of the inventors of the present application to avoid the use of toxic reactants or reduce such reactants to a minimum. As noted above, an additional objective was to involve a minimum of reactants in the process. The solution taught by Buddy is therefore not within the objectives of the present invention. In fact, Buddy teaches one of ordinary skill in the art who desires to improve the process taught by Dazzi in an entirely different direction than the present invention, i.e. Buddy teaches away from the present invention.

Contrary to the teachings in Dazzi and Budsky, the inventors of the present application surprisingly found that it was possible to reduce the amount of pyridine from the amount taught by Dazzi without employing further reactants and solvents in the reaction and still maintain a high yield and to keep the reaction time and temperature within controllable limits. Applicants therefore strongly disagree that the combined teachings of Budsky and Dazzi makes it obvious to one skilled in the art to reduce the amount of pyridine in the reaction to the amounts claimed in the attached claims.

Applicants were also aware of the technology described by Gibby prior to the present invention and direct the Examiner's attention to page 1, lines 29 to 32 of the description in the present application (published international application WO 2005/058846). Applicants therefore concur with the Examiner that at the time of the invention it was obvious to one ordinarily skilled in the art to produce DTPA-bis(anhydride) by reacting DTPA with a molar amount of anhydrous acetic acid four times that of DTPA and a molar amount of pyridine that is 6.2 times that of DTPA at 65°C for 20h without the use of acetonitrile as disclosed in col. 4, Example 1. With regard to the calculated molar amount to 6.2 of pyridine, applicant refers to the calculation of the amounts of Example 1 of Gibby which was enclosed in applicants response to the Office Action dated February 28, 2008.

For the same reasons as argued above regarding the combined teachings of Dazzi and Budsky, applicants strongly disagree that the combined teachings of Budsky and Gibby makes it obvious to one skilled in the art to reduce the amount of pyridine in the reaction to the amounts claimed in the attached claims.

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Applicants now believe that claims 1, 2, 6-11 and 13-15 are in condition for allowance and respectfully request that the Examiner's rejections for these claims under 35 USC §103 (a) be withdrawn.

### **CONCLUSION**

In view of the amendments and remarks herein, Applicants believe that each ground for rejection made in the present application has been successfully overcome, and that all the pending claims, 1-16, are in condition for allowance.

The Examiner is invited to telephone the undersigned in order to resolve any issues that might arise and to promote the efficient examination of the current application.

Respectfully submitted,

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